UNITED STATES PATENT AND TRADEMARK OFFICE

CERTIFICATE OF CORRECTION

PATENT NO. : 7,157,418 B1
APPLICATION NO. : 09/360242
DATED : January 2, 2007
INVENTOR(S) : John R. McDonald and Phillip J. Coggins

It is certified that error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

IN THE TITLE PAGES:

In Item [57] ABSTRACT, line 1 please delete the "a" between "ligand" and "chemokine"

in Item [57] ABSTRACT, please replace "neutrophiles" with --neutrophils--

in Item [56] *References Cited* please add to the list of OTHER PUBLICATIONS --Kreitman and Pastan, *Semin. Cancer Biol.* *6*(5):297-306 (1995).--

in Item [56] *References Cited* please add to the list of OTHER PUBLICATIONS --Kreitman, R.J., et al., Recombinant toxins, *Adv. Pharmacol., 28*:193-219 (1994).--

in Item [56] *References Cited* please add to the list of OTHER PUBLICATIONS --Medh, J.D., et al., *J. Biol. Chem., 270:*536-540 (1995).--

in Item [56] *References Cited* please add to the list of OTHER PUBLICATIONS --Puri, *Toxicol. Pathol. 27*:53-57 (1999).--

in Item [56] *References Cited* please add to the list of OTHER PUBLICATIONS --Sawada, M., et al., *Neurosci. Lett., 160*:131-4 (1993).--

in Item [56] *References Cited* please add to the list of OTHER PUBLICATIONS --Stirpe, F., et al., *J. Biol. Chem., 255*:6947-6953 (1980).--

in Item [56] *References Cited* please add to the list of OTHER PUBLICATIONS --Ugoccioni, M., et al., *J. Exp. Med., 183*:2379-84 (1996).--

in Item [56] *References Cited* please add to the list of OTHER PUBLICATIONS --Zheng, G., et al., *J. Histochem. Cytochem., 42*: 531-42 (1994).--

in Item [56] *References Cited*, in OTHER PUBLICATIONS: in EMBL database ID HS1301003, please replace "(Lingkine)" with --(Lungkine)--

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in Hesselgesser et al., please replace "Chernokine" with --Chemokine--
in Richmond et al., please replace "chernokine/chernokine receptor" with --chemokine/chemokine receptor--
in Signoret et al., please replace "Chernokine" with --Chemokine--

IN THE SPECIFICATION:

At column 1, line 24, please insert --FIELD OF THE INVENTION The present invention relates to therapeutic compositions and their use in treatment of disease states. More particularly, compounds, compositions and methods for treating disease states associated with proliferation, migration and physiological activity of cells involved in inflammatory responses, including, but not limited to, secondary tissue damage, are provided.--
at column 14, line 43, please replace "FIG. 1 is a schematic drawing" with --FIG. 1A-1C presents schematic drawings--
at column 14, line 56, please insert --(also designated herein pOPL2)-- between "pGEMEX-SAP" and "encoding"
at column 14, lines 59-60, please replace "map of a conjugate MCP-3-AM-Shiga-A1" with --map of a plasmid, designated pOPL1, encoding the conjugate MCP-3-AM Shiga-A1, which was--
at column 14, lines 62-63, please replace "map of a conjugate MCP-1-AM-SAP" with --map of a plasmid, designated pOPL106, encoding the conjugate MCP-1-AM-SAP--
at column 14, lines 65-66, please replace "map of a conjugate MCP3-AM-Shiga-A1" with --map of a plasmid, designated pOPL101, encoding the conjugate MCP-3-AM Shiga-A1--
at column 16, line 56, please delete "ALP,"
at column 32, line 25, please delete "of"
at column 57, line 30, please insert --)-- between "1986" and "."
at column 57, line 51, please replace "Ed." with --ed.--
at column 68, line 56, please replace "MIP-1 alpha" with --MIP-1α--
at column 69, line 13, please insert --which-- between "mice" and "predictably"

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IN THE CLAIMS:

Please replace Claims 5, 11, 18, 20, 25, 27, 28, 31, 32, 40, 45, 48, 50 and 55 with the following Claims:

5. The method of claim 1, wherein the activated, proliferating or migrating immune cells occur in a disorder or disease state that is selected from the group consisting of CNS injury, CNS inflammatory diseases, neurodegenerative disorders, heart disease, inflammatory eye diseases, inflammatory bowel diseases, inflammatory joint diseases, inflammatory kidney or renal diseases, inflammatory lung diseases, inflammatory nasal diseases, inflammatory thyroid diseases, inflammatory responses associated with bacterial or viral infections and cytokine-regulated cancers.

11. The method of claim 1, wherein the conjugate comprises the following components: (chemokine receptor targeting agent)$_n$, (L)$_q$ and (targeted agent)$_m$,

wherein: L is a linker for linking the chemokine receptor targeting agent to a targeted agent; chemokine receptor targeting agent is any moiety that selectively binds to a chemokine receptor and effects internalization of the conjugate;

m and n, which are selected independently, are at least 1; and

q is 0 or more as long as the resulting conjugate binds to the targeted receptor, is internalized and delivers the targeted agent;

the resulting conjugate binds to a receptor that interacts with and internalizes a chemokine, whereby the targeted agent(s) is internalized in a cell bearing the receptor; and

when the conjugate contains a plurality of targeted agents, the targeted agents are the same or different, and when the conjugate contains a plurality of chemokine receptor targeting agents, the targeting agents are the same or different.

18. The method of claim 11, wherein the chemokine receptor targeting agent and targeted agent are linked directly via a covalent or ionic linkage.

20. The method of claim 19, wherein the linker is a peptide linkage, a polypeptide or a chemical linker.

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25. The method of claim 22, wherein the chemokine is selected from the group consisting of IL-8, GCP-2, GRO-α, GRO-β, GRP-γ, ENA-78, PBP, CTAP III, NAP-2, LAPF-4, MIG, IP-10, SDF-1α, SDF-1β, SDF-2, MCP-1, MCP-2, MCP-3, MCP-4, MCP-5, MIP-1α, MIP-1β, MIP-1γ, MIP-2, MIP-2α, MIP-3α, MIP-3β, MIP-4, MIP-5, MDC, HCC-1, LD78β, eotaxin-1, eotaxin-2, I-309, SCYA17, TARC, RANTES, DC-CK-1, lymphotactin and fractalkine.

27. The method of claim 1, wherein the chemokine receptor is selected from the group consisting of CXCR-1, CXCR-2, CXCR-3, CXCR-4, CXCR-5, CCR-1, CCR-2A, CCR-2B, CCR-3, CCR-4, CCR-5, CCR-6, CCR-7, CCR-8, CX3CR-1, XCR1, Duffy antigen receptor for chemokines (DARC) and CD97.

28. The method of claim 22, wherein the chemokine receptor is selected from the group consisting of DARC, CXCR-1, CXCR-2, CXCR-3, CXCR-4, CCR-1, CCR-2A, CCR-2B, CCR-3, CCR-4, CCR-5, CCR-6, CCR-7, CCR-8, CX3CR-1, and CD97.

31. A method for inhibiting proliferation or migration of activated immune effector cells, comprising contacting immune effector cells with a conjugate that comprises a targeted agent or a portion thereof and a chemokine receptor targeting agent, whereby activation or proliferation of the immune effector cells is nhibited, wherein:

the targeted agent or portion thereof is a toxin;

the chemokine receptor targeting agent is a chemokine or a fragment thereof that binds to a chemokine receptor and internalizes the targeted agent; and

the conjugate binds to a chemokine receptor resulting in internalization of the targeted agent in cells bearing the receptor.

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32. The method of claim 31, wherein the conjugate comprises the following components: (chemokine receptor targeting agent)$_n$, (L)$_q$ and (targeted agent)$_m$,

wherein: L is a linker for linking the chemokine or fragment thereof to a targeted agent;

m and n, which are selected independently, are at least 1; and

q is 0 or more as long as the resulting conjugate binds to the targeted receptor, is internalized and delivers the targeted agent;

the resulting conjugate binds to a receptor that interacts with and internalizes a chemokine, whereby the targeted agent(s) is internalized in a cell bearing the receptor; and

when the conjugate contains a plurality of targeted agents, the targeted agents are the same or different, and when the conjugate contains a plurality of chemokine receptor targeting agents, the targeting agents are the same or different.

40. The method of claim 29, wherein the chemokine is selected from the group consisting of IL-8, GCP-2, GRO-α, GRO-β, GRP-γ, ENA-78, PBP, CTAP III, NAP-2, LAPF-4, MIG, IP-10, SDF-1α, SDF-1β, SDF-2, MCP-1, MCP-2, MCP-3, MCP-4, MCP-5, MIP-1α, MIP-1β, MIP-1γ, MIP-2, MIP-2α, MIP-3α, MIP-3β, MIP-4, MIP-5, MDC, HCC-1, LD78β, eotaxin-1, eotaxin-2, I-309, SCYA17, TARC, RANTES, DC-CK-1, lymphotactin, and fractalkine.

45. A method of preparing a candidate compound for treating a disease or disorder involving activated immune cells, comprising:

identifying immune cells that are activated in the disease or disorder;

identifying chemokine receptors expressed on the cells; and

preparing a conjugate or plurality thereof containing a toxin linked to a chemokine or a plurality of chemokines that specifically bind to the identified chemokine receptors and effect or facilitate internalization of the toxin into the cells.

48. The method of claim 21, wherein the chemokine receptor targeting agent is selected from the group consisting of IL-8, GCP-2, GRO-α, GRO-β, GRP-γ, ENA-78, PBP, CTAP III, NAP-2, LAPF-4, MIG, IP-10, SDF-1α, SDF-1β, SDF-2, MCP-1, MCP-2, MCP-3, MCP-4, MCP-5, MIP-1α, MIP-1β, MIP-1γ, MIP-2, MIP-2α, MIP-3α, MIP-3β, MIP-4, MIP-5, MDC, HCC-1, LD78β, eotaxin-1, eotaxin-2, I-309, SCYA17, TARC, RANTES, DC-CK-1, lymphotactin, and fractalkine.

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50. The method of claim 45, wherein the chemokine is selected from the group consisting of IL-8,GCP-2, GRO-α, GRO-β, GRP-γ, ENA-78, PBP, CTAP III, NAP-2, LAPF-4, MIG, IP-10, SDF-1α, SDF-1β, SDF-2, MCP-1, MCP-2, MCP-3, MCP-4, MCP-5, MIP-1α, MIP-1β, MIP-1γ, MIP-2, MIP-2α, MIP-3α, MIP-3β, MIP-4, MIP-5, MDC, HCC-1, LD78β, eotaxin-1, eotaxin-2, I-309, SCYA17, TARC, RANTES, DC-CK-1, lymphotactin, and fractalkine.

55. The method of claim 45, further comprising:

contacting the immune cells with the conjugate or plurality thereof, whereby the toxin is internalized.

Signed and Sealed this

Eighteenth Day of March, 2008

JON W. DUDAS
Director of the United States Patent and Trademark Office